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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/526,260

12/22/2005

Conan J. Fee

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER

SAKELARIS, SALLY A

ART UNIT

PAPER NUMBER

1797

NOTIFICATION DATE

DELIVERY MODE

04/30/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com

eOAPilot@kmob.com

Office Action Summary	Application No. 10/526,260	Applicant(s) FEE, CONAN J.	
	Examiner Sally A. Sakelaris	Art Unit 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26, 28 and 29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-26, 28 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/22/2005</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-3, 5, 6, 11-18, 20, 21, 25, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilding et al.(US Patent 5637469).

Wilding et al teach reaction processes for detecting the presence of a preselected analyte in a fluid sample. Depending on the reactions and the composition of the reaction components, a different flow rate exists. Red blood cells for instance will have a flow rate of zero through the substrate when they are trapped within the filter, unlike the surrounding fluid or contents of red blood cells that have become freed following the cells rupture (via 124). Reaction products are numerous with varied characteristics as they could merely be a purified sample free of cellular debris or alternatively they could be nucleic acids that will undergo PCR. The devices comprise a substrate microfabricated to define a sample inlet port, and a mesoscale flow system that includes a sample flow channel extending from the inlet port. The mesoscale flow system further includes an analyte detection region in fluid communication with the flow channel comprised of a binding moiety for specifically binding the analyte. The detection region is constructed with a mesoscale dimension sufficiently small to enhance binding of the binding moiety and the analyte. The binding moiety may be

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immobilized in the detection region. The mesoscale detection systems of the invention may be used in a wide range of applications, including the detection of cells or macromolecules, or for monitoring reactions or cell culture growth. Sample flow continues past filter 168, which filters off large cellular membranes and other debris, to the mesoscale PCR chambers 164 and 166. The appliance 50 is provided with flow paths 56 mated to ports 16A-D. Reagents such as primers, nucleoside triphosphates, and Taq polymerase may be added to the polynucleotide sample before delivery through inlet port 16A, or optionally, reagents may be delivered to the sample in sample chambers 164 and 166 via port 16C by means of the appliance. After delivery of a sample to PCR reaction chambers 164 and 166, the appliance is utilized to shut ports 16A and 16D. Port 16C remains open as a vent. A pump disposed in appliance 50 is then utilized to cycle fluid between chamber 164, heated to 94.degree. C., for polynucleotide dehybridization, and chamber 166, heated to 65.degree. C., for the polymerization reaction.

2. Claims 1-6 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomas et al. (PNAS April 24, 2001, Vol.98, no.9 pgs 4932-4937).

Thomas et al. teaches a reaction process involved in their DIOS mass spectrometry platform to characterize proteins. The medium is the mass spectrometry environment where intact gas phase ions are formed and UV laser light desorbs intact analytes from the surface. DIOS-MS is used not only for the identification and functional characterization of proteins but also for the identification of reaction products resulting

from protein-catalyzed chemical transformations. The movement and flow rates of the reaction components through the medium of the electromagnetic field is dependent on each ionized chemical compound's electrostatic charge and mass via measurement of their mass-to-charge ratio. The reaction products are finally separated for their identification within and following their flow through the electromagnetic medium. The flow of ionized particles can be affected by changing the properties of the nitrogen laser's beam column of light and reflection mirror.

3. Claims 1, 2, 6, 7, 11-16, 21 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Alesandrini et al. (EP 0142103 B1).

Alesandrini teaches a reaction process in a multi-tubular vessel containing a plurality of packed vertically arranged tubes (Figures 3-6). The process is taught to contain at least one liquid that has been introduced into the tubular zone and results in at least one liquid product and at least one gaseous product being obtained (Col. 1 lines 11-12). There is a different flow rate from tube to tube. The tubes with the most reaction, and therefore the greatest rate of gas generation, will have the lowest pressure drop, which is dependent on the proportion of gas to liquid within each tube. More feed therefore will flow to these tubes, which then generate gas faster, and experience a temperature rise, and because of the low pressure drop, liquid will feed quicker to these tubes than to the others (Col. 2 lines 50-65). Alesandrini et al attempt to control for this variant flow rates by "removing a liquid product from the lower portion of the vessel in a controlled manner so as to maintain the level of liquid in the vessel above the upper

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ends of the tubes substantially throughout the interior of the vessel" (Col. 3 lines 48-52).

The variant flow rate of the reaction components through the medium can also be interpreted as the variant flow of liquid and gas through the columns as affected by the column medium.

With regard to claims 6, 7, 11-13, the process is carried out in a vertically situated vessel or reactor filled with tubes, designated generally as 21. In the upper portion of the vessel 21 is a liquid/vapor disengagement zone 23. The tubes are essentially packed from top to bottom with particulate solid material. If the chemical process to be carried out is enhanced by the use of a catalyst, the particulate material may contain catalytic material, either *per se*, or supported on an inert particulate support. If the process to be carried out does not require the presence of a catalyst, the particulate material may be some inert material which enhances in some other way the conduct of the process, for instance a packing, an adsorbent, an ion exchange resin, etc.(Col. 4 lines 20-35). Liquid chlorothioformate is produced by reaction of a liquid mercaptan with phosgene.

With regard to claims 14 and 15, the reaction products, both liquid and gas are selectively removed as a result of their molecular weight throughout the process in the tubular zone. Alesandrini teaches that removal in a controlled manner as described results not only in the flooding the tubes with liquid, thus maintaining uniformity of flow, but in causing the gas product to pass upwards through the tubes and out the reactor via line 24 rather than downwardly or along with the liquid in the outlet line 25.

With regard to claim 16, the medium of activated carbon catalysts were chosen to complete the process in favor of liquid chlorothioformate being produced versus other products.

With regard to claim 21, portions of phosgene's bonds are cleaved by liquid mercaptan in the process (Col. 6 line. 33-35).

With regard to claim 25, a final desired liquid product, chlorothioformate, is obtained and withdrawn via line 28. (Col. 4, lines 53-55).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
4. Claims 3-5, 8-10, 17,18, 20, 22-24, 28, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alesandrini et al. (EP 0142103 B1) in view of Abbott et al. (US Patent 6277489).

Alesandrini's teachings can be seen above.

Alesandrini does not teach the particular constituent parts and attributes of the medium to be loaded into his columns, PEGylation methods, or kits.

With regard to claims 3-5 and 23, Abbott et al. teach multilayered particulate materials comprising various moieties that are capable of interacting with various analytes of interest for their detection, purification, modification, etc. The novel particulate materials taught by Abbott can be utilized in methods including ion exchange, affinity dialysis, size exclusion dialysis, as supports in solid phase synthesis, combinatorial synthesis and the like.

With regard to claims 8-9, Abbott teaches the used of Sepahdex® columns which are cross-linked dextrans in their affinity chromatography examples (Col. 45 line 23 and Col. 27 lines 26-44).

With regard to claim 10, Abbott teaches colloidal matrices that include silica, gel, agar, agarose, and cross linked dextrans (Col. 45 lines 20-26 and Col. 25 line 40).

With regard to claims 17 and 18, the reaction process' specificity is taught throughout the reference but one example of such orientation for multiple active sites and chemical protection is taught in Col 45 and 46 where the compounds are cleaved after the beads are embedded in the colloidal matrix, it is preferred to use photolysis. By adjusting light exposure, it is possible to control the amount of compound that diffuses in the matrix. If more light is applied, more cleavage results, releasing more compound into the matrix. This allows the amount of active compound released to be

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adjusted, so that zones of activity are only produced for compounds that are most active. (Col. 46 lines 23-34).

With regard claims 28 and 29, Abbott et al. teach a kits for practicing the methods of the invention and the kits can include any of the compositions noted and instructions to practice the methods (Col. 54 lines 7-14).

Therefore, it would have been obvious with regard to claims 3-5, 8-10, 17, 18, 23, 28 and 29 to one of ordinary skill in the art at the time the invention was made to have adopted the particular beads, and solid supports of Abbott within the columns of Alesandrini as chromatographic methods are well known in the art and would have provided a "substantially homogeneous, easily assembled organic layer that does not adventitiously and/or nonspecifically bind charged species"(Col. 3 lines 56-61).

With regard to claims 20, 22 and 24 Abbott teaches that in a preferred embodiment of their multilayered particulate, the organic layer includes both charged and uncharged hydrophilic polymers of various weights including poly(ethyleneglycol) (PEG). Abbott further teaches that many methods are available in the art for attaching poly(ethyleneglycol) moieties to other molecules but teach in their method to effect covalent attachment of PEG to another molecule, for example, a protein, the hydroxyl end-groups of the polymer are first converted into reactive functional groups and that these activated PEG derivatives be used within columns made of their multilayered particulate materials (Col. 15 lines 15-41).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have added Abbott's activated PEG moiety-laden

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particulates to the columns of Alesandrini as proteins treated with PEG have been shown to resist protein deposition and have improved resistance to thrombogenicity and since “many methods are available in the art for attaching PEG moieties to other molecules”.

5. Claims 19 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alesandrini et al. (EP 0142103 B1) in view of Abbott et al. (US Patent 6277489) and in further view of Burg et al. (US Patent 7128913).

The teachings of Alesandrini in view of Abbot can be seen above.

The modified Alesandrini in view of Abbott do not teach the process including glycosylation or reaction products that include a PEGylated protein.

Burg et al. teach a size exclusion chromatography method on agarose and dextran crosslinked beads that both glycosylates (Col. 6 lines 44-55) and PEGylates the protein erythropoietin (EPO) (Example 3, Col. 17-18). The separation of N-terminal pegylated EPO (PEG-A1-EPO) from excess reagents, reaction byproducts and nonpgylated EPO was achieved by chromatography on SP-Sepahrose FF. The PEG-A1-EPO pool was then concentrated and kept in storage buffer (Col. 18 lines 17-19).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the teachings of Alesandrini and Abbott in view of Burg as there exists a need for a pegylated compostion that is essentially comprised of a single positional isomer of a protein and that this can readily be synthesized with current state of the art production-scale technology.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sally A. Sakelaris whose telephone number is 5712726297. The examiner can normally be reached on Monday-Friday 8-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 5712721267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sally Sakelaris

/Jill Warden/
Supervisory Patent Examiner, Art Unit 1797